

Amendment and Response Under 37 C.F.R. §1.116 - Expedited Examining Procedure

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Serial No.: 09/847,670

Confirmation No.: 4815

Filed: May 2, 2001

For: HEPATITIS C VIRUS HELICASE CRYSTALS, CRYSTALLOGRAPHIC STRUCTURE AND METHODSAmendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1-30. (Canceled)

31. (Withdrawn - Currently Amended) A method for crystallizing [[a]] Hepatitis C virus helicase molecule or molecular complex comprising growing a crystal from a precipitant solution comprising purified Hepatitis C virus helicase, about 3% by weight to about 14% by weight PEG, about 5% by weight to about 15% by weight DMSO, and about 0.05M to about 0.07M potassium phosphate, wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.

32-34. (Canceled)

35. (Withdrawn - Currently Amended) A method for crystallizing [[a]] Hepatitis C virus helicase molecule or molecular complex comprising growing a crystal by vapor diffusion with macro-seeding from a precipitant solution comprising purified Hepatitis C virus helicase, HEPES, and about 4% by weight to about 14% by weight mono-alkyl ether of PEG, wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.

36-37. (Canceled)

38. (Original) Crystalline Hepatitis C virus helicase comprising a tetragonal crystal having unit cell dimensions of $a = b = 109 \text{ \AA} \pm 3 \text{ \AA}$; $c = 84 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and space group $P4_1$; the unit cell containing two molecules in an asymmetric unit.

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39. **(Previously Presented)** The crystalline Hepatitis C virus helicase of claim 38 wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.
40. **(Original)** Crystalline Hepatitis C virus helicase comprising an orthorhombic crystal characterized by unit cell dimensions of $a = 66 \text{ \AA} \pm 2 \text{ \AA}$; $b = 110 \text{ \AA} \pm 3 \text{ \AA}$; $c = 64 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and a space group $P2_12_12_1$; the unit cell containing one molecule in the asymmetric unit.
41. **(Previously Presented)** The crystalline Hepatitis C virus helicase of claim 40 wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.
42. **(Currently Amended)** Crystalline Hepatitis C virus helicase having amino acid sequence SEQ ID NO:1, wherein the crystalline Hepatitis C virus helicase effectively diffracts x-rays to a resolution of 1.5 \AA to 3 \AA.
43. **(Currently Amended)** A composition comprising crystalline Hepatitis C virus helicase of any of claims 38-41 ~~claims 38-42~~.
- 44-46. **(Canceled)**
47. **(Withdrawn - Currently Amended)** A method for incorporating a chemical entity in a crystal comprising placing a tetragonal crystal of Hepatitis C virus helicase having unit cell dimensions of $a = b = 109 \text{ \AA} \pm 3 \text{ \AA}$; $c = 84 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; the unit cell containing two molecules in an asymmetric unit; and space group $P4_1$ in an aqueous solution comprising about 1mM to about 10mM chemical entity, and 0% by weight to about 15% by weight DMSO.
48. **(Withdrawn - Currently Amended)** A method for incorporating a chemical entity in a crystal comprising placing an orthorhombic crystal of Hepatitis C virus helicase having unit cell

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dimensions of $a = 66 \text{ \AA} \pm 2 \text{ \AA}$; $b = 110 \text{ \AA} \pm 3 \text{ \AA}$; $c = 64 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; the unit cell containing one molecule in the asymmetric unit; and a space group $P2_12_12$ in an aqueous solution comprising about 1mM to about 10mM chemical entity, and 0% by weight to about 15% by weight DMSO.

49. (Currently Amended) Crystalline Hepatitis C virus helicase wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1, and wherein the crystalline Hepatitis C virus helicase effectively diffracts x-rays to a resolution of 1.5 \AA to 3 \AA.

50. (Currently Amended) A crystal of Hepatitis C virus helicase, wherein the Hepatitis C virus helicase comprises amino acid sequence SEQ ID NO:1, and wherein the crystal effectively diffracts x-rays to a resolution of 1.5 \AA to 3 \AA.

51. (Currently Amended) A crystal of Hepatitis C virus helicase, wherein the Hepatitis C virus helicase comprises amino acid sequence SEQ ID NO:1, with the proviso that at least one cysteine or methionine is replaced with selenocysteine or selenomethionine, respectively, and wherein the crystal effectively diffracts x-rays to a resolution of 1.5 \AA to 3 \AA.

52. (Currently Amended) A crystal of Hepatitis C virus helicase, wherein the Hepatitis C virus helicase consists of amino acid sequence SEQ ID NO:1, and wherein the crystal effectively diffracts x-rays to a resolution of 1.5 \AA to 3 \AA.

53. (Previously Presented) A crystal of Hepatitis C virus helicase comprising a unit cell having dimensions of $a = b = 109 \text{ \AA} \pm 3 \text{ \AA}$; $c = 84 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and space group $P4_1$; the unit cell containing two molecules in an asymmetric unit.

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54. **(Previously Presented)** A crystal of Hepatitis C virus helicase comprising a unit cell having dimensions of $a = 66 \text{ \AA} \pm 2 \text{ \AA}$; $b = 110 \text{ \AA} \pm 3 \text{ \AA}$; $c = 64 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and a space group $P2_12_12_1$; the unit cell containing one molecule in the asymmetric unit.
55. **(Previously Presented)** A crystal of Hepatitis C virus helicase comprising atoms arranged in a spatial relationship represented by the structure coordinates listed in Table 1.
56. **(Previously Presented)** A crystal of Hepatitis C virus helicase comprising atoms arranged in a spatial relationship represented by the structure coordinates listed in Table 2.
57. **(Previously Presented)** A crystal of Hepatitis C virus helicase comprising atoms arranged in a spatial relationship represented by the structure coordinates listed in Table 3.
58. **(Currently Amended)** A crystal of Hepatitis C virus helicase prepared by a method comprising growing a crystal from a precipitant solution comprising purified Hepatitis C virus helicase, about 3% by weight to about 14% by weight PEG, about 5% by weight to about 15% by weight DMSO, and about 0.05M to about 0.07M potassium phosphate, wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.
59. **(Currently Amended)** A crystal of Hepatitis C virus helicase prepared by a method comprising growing a crystal by vapor diffusion with macro-seeding from a precipitant solution comprising purified Hepatitis C virus helicase, HEPES, and about 4% by weight to about 14% by weight mono-alkyl ether of PEG, wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1.
60. **(New)** A crystal of Hepatitis C virus helicase, wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1, and wherein the crystal is about $0.12 \times 0.12 \times 0.05$ mm in size.

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61. (New) A crystal of Hepatitis C virus helicase, wherein the amino acid sequence of the Hepatitis C virus helicase is SEQ ID NO:1, and wherein the crystal is about 0.4 x 0.4 x 0.2 mm in size.